Applicants have amended claim 34 to clarify that the method is suitable for determining the presence of target nucleic acids.

Title

Applicants have submitted a new title.

Double Patenting

Applicants have enclosed a Terminal Disclaimer over U.S. Pat. 5,744,299.

§ 103 Rejection

Claims 34 - 36 are rejected under 35 U.S.C. § 103(a) as unpatentable over Karron, et al. (J. Clinical Micro. 32(2):484-488, 1994) in view of Sninsky, et al. (U.S. Pat. 5,176,995). Although the Examiner has not included Wu, et al., in lines 3 and 4 on page 6 of the Office Action, Applicants note that the Examiner uses Wu, et al. in a combination with Karron and Sninsky to discuss his combination. (Applicants note line 15 where the Examiner notes that "one . . . would have been motivated to apply Wu, et al.'s primer . . . .") Therefore, Applicants have responded as if Wu, et al. were part of the combination initially cited in paragraph 8.

Applicants agree that Karron, et al. teach PCR rapid detection of HPIV-3 and that Sninsky, et al. teach

detection by hybridizing with a probe that is complementary to conserved nucleic acid sequence of the genome of a virus. The Examiner uses Wu, et al. to "teach a method a of performing polymerase chain reaction using unequal primer concentration in which the primer pairs are at least 2:1." Applicants strenuously protest the characterization of the references as teaching the present invention.

Applicants have commented on the Wu, et al. reference before, most notably in a response dated May 7, 1999 in related application Serial No. 08/691,045. In that response, Applicants attached a Declaration of Dr. Kelly Henrickson and Dr. Jiang Fan, in response to the above-identified application, noting that the Wu, et al. application does not describe PCR reactions in which the product is double-stranded. Applicants have amended all claims to emphasize that the reaction product is a double-stranded molecule.

In brief, Applicants assert that the Wu, et al. application does not describe PCR reaction in which "the product is double-stranded." Dr. Henrickson and Dr. Fan point out that Wu, et al. is drawn to asymmetric PCR that results in single-stranded molecules. Note that the Wu, et al. reference describes amplification wherein "denaturation of the complementary products prior to

detection is not needed." Wu, et al. cannot be combined with the other references to teach the suitability of unequal primer concentration in multiplex determinations because Wu, et al. does not teach the production of double-stranded products.

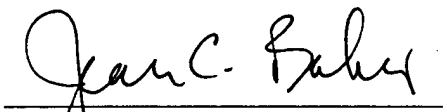
In summary, the Examiner's cited references do not disclose a method of detecting target nucleic acids using Applicants' unequal primer concentration method.

Applicants believe the claims to be allowable and respectfully request a Notice of Allowance. A Petition and Fee for Three Months Extension of Time is enclosed. If further fees are necessary, please charge Deposit Account 17-0055.

Respectfully submitted,

Kelly J. Henrickson, et al.

February 7, 2002

By: 

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Kelly J. Henrickson, et al.
Serial No.:	09/484,704
Filed:	January 18, 2000
For:	VIRUS ASSAY METHOD
Group Art Unit:	1656
Examiner:	J. Siew

Commissioner For Patents
Washington, D.C. 20231

MARKED UP VERSION OF THE CLAIMS

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34. (Amended) A method of detecting the presence of a target nucleic acid [virus infection] in a biological sample comprising the steps of

(a) isolating nucleic acid from a biological sample,

(b) exposing the nucleic acid or cDNA created from the nucleic acid to at least one primer pair, comprising a 5' and a 3' primer, specific for [at least one human virus] the target nucleic acid under conditions suitable for nucleic acid amplification and wherein the 5' and 3' primers are of unequal concentration, wherein [an] a double-stranded amplification product is formed if the sample contains [any of the at least one virus] the target nucleic acid, and

(c) determining whether the amplification product is present by exposing the step (b) products to

protein-linked oligonucleotide probes under conditions suitable for hybridization between complementary nucleic acid sequences and examining the probes for the presence of a hybridization product, wherein the oligonucleotide probe is of a sequence identical to a [viral sequence] the target nucleic acid.